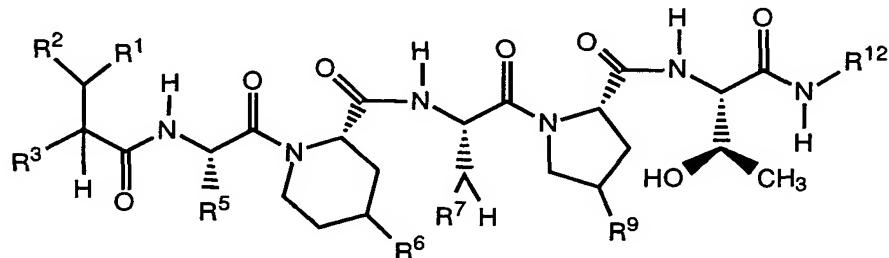


PIPECOLIC ACID DERIVATIVES OF PROLINE THREONINE  
AMIDES USEFUL FOR THE TREATMENT OF RHEUMATOID  
ARTHRITIS

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ABSTRACT

Non-peptidic compounds characterized by containing a segment condensed from pipecolic acid, aspartic acid, proline and threonine, or derivatives thereof, are 10 useful to treat autoimmune diseases and inflammatory conditions. Compounds of particular interest are those of the formula:



wherein R<sup>1</sup> is phenyl or cyclohexyl; wherein R<sup>2</sup> is hydrido or 15 methyl; wherein R<sup>3</sup> is selected from hydrido, hydroxy, acetylamino, acetyl(Lys/Tyr/Thr)NH-, propionylamino and benzyloxycarbonylamino; wherein R<sup>5</sup> is selected from isopropyl, isobutyl, n-propyl, n-butyl, aminopropyl, aminobutyl, phenyl, benzyl, hydroxyphenyl, hydroxybenzyl, 20 morpholinocarbonyl, morpholinocarbonylpropyl, piperazinocarbonyl, piperazinocarbonylpropyl, pyridinylcarbonyl, pyridinylcarbonylpropyl, oxazolylcarbonyl, oxazolylcarbonylpropyl, azepinylcarbonyl, and azepinylcarbonylpropyl; wherein R<sup>6</sup> is selected from hydrido, methyl, hydroxy, methoxy, phenyl and aminocarbonyl; wherein R<sup>7</sup> is carboxyl or methylthiomethyl; wherein R<sup>9</sup> is selected from hydrido, hydroxy, methoxy and phenyl; wherein R<sup>12</sup> is selected from methyl, ethyl, propyl, butyl, isobutyl, -CH(iBu)CH<sub>2</sub>OH and 25 -CH(iBu)CONH<sub>2</sub>; or a pharmaceutically-acceptable amide, ester or salt thereof. A disease state of particular interest for use of the compounds would be rheumatoid 30 arthritis.